REMARKS

This document is submitted in response to the Office Action of May 25, 2006. In the May 25, 2006 Office Action claims 1, 5-21, and 77-100 were subject to a restriction and/or election requirement and claims 1, 5-21 and 77-96 were rejected under 35 U.S.C. §102(b) and §103(a). Each of these is addressed below.

Election/Restriction Requirement

In the Office Action mailed May 25, 2006, the Examiner required that the claims be restricted to one of the following inventions:

I. Claims 1, 5-21, 77-96, drawn to methods of aptamer formation, classified in claims 435, subclass 6.

II. Claims 97-100, drawn to aptamers, classified in class 536, subclass 23.1.

Applicant hereby confirms the provisional election made without traverse, on March 28, 2006, by Jennifer Karnakis, during a telephone conversation with the Examiner, to prosecute the invention of Group 1, claims 1, 5-21 and 77-96.

Claim Interpretation

The Examiner states that in claim 1, the phrase "mutated polymerase" is used but that there is no particular structure assigned in claim 1 to the mutated polymerase. The Examiner goes on to state that in fact the term "mutated" simply implies that the polymerase is changed relative to another polymerase sequence. The Examiner then states that there are two issues with regards to the "mutated" limitation in claim 1 of the pending application. The Examiner states that "First, there is the issue of written description, as discussed more fully in that rejection." There is, however, no written description rejection in the office action mailed May 25, 2006 which is the first substantive office action received in relation to this application.

The Examiner states that "Second, the claim is interpreted broadly as reading on any polymerase, since any polymerase may be interpreted as "mutated" as relative to some other polymerase." Applicant respectfully disagrees.

It is never appropriate to rely solely on "common knowledge" in the art without evidentiary support in the record, as the principal evidence upon which a rejection was based. *In re Zurko*, 258 F.3d 1379, 1385 (Fed. Cir. 2001) ("[T]he Board cannot simply reach conclusions based on its own understanding or experience-or on its assessment of what would be basic knowledge or common sense. Rather the Board must point to some concrete evidence in the record in support of these findings.").

The Examiner does not cite any evidentiary support in the record for the statement that in fact the term "mutated" simply implies that the polymerase is changed relative to another polymerase sequence. Furthermore, a person skilled in the art would understand that the mutated polymerase of claim 1 is mutated relative to the wild type polymerase. A person of skill in the art would not understand the term mutated polymerase to read on any polymerase whatsoever including, for example, wild type polymerases. Accordingly, the term "mutated polymerase" as used in claim 1 is not broad enough to read on any polymerase, rather it encompasses a polymerase mutated relative to the corresponding wild type polymerase.

To the extent that the Examiner is relying on personal knowledge to support the finding of what "mutated polymerase" is understood to mean in the art, Applicant requests that the Examiner provide an affidavit or declaration setting forth specific factual statements and explanation in support pursuant to 37 CFR 1.104(d)(2).

Rejection under 35 U.S.C. §102(b)

The Court of Appeals of the Federal Circuit has stated that anticipation requires the presence in a single prior art reference of each and every element of the claimed invention. Lindemann Maschinenfabrik GMBH v. American Hoist &Derrick Co., 730 F. 2d 1452, 1458 (Fed Cir. 1984); Alco Standard Corp. v. Tennessee Valley Auth., 1 USPQ2d 1337, 1341 (Fed. Cir. 1986) "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. Scripps Clinic v. Genentech, Inc., 18 USPQ2d 1001, 1010 (Fed. Cir. 1991) (citations omitted).

The Examiner has rejected claims 1, 5, 9-11, 17, 19-22, 77 and 78 under 35 U.S.C. §102(b) as being anticipated by Pieken et al. U.S. Patent No. 5,660,985 (the '985 patent). As an initial matter, Applicant points out that claim 22 is no longer pending in the application. The Examiner states that the '985 patent teaches a method of claim 1. In arriving at this conclusion, the Examiner deletes the "mutated" limitation prior to the word polymerase at each point in the analysis at which the "mutated polymerase" limitation appears in pending claim 1. As discussed above, however, a person of ordinary skill in the field of the present invention would not understand claim 1 to encompass any polymerase whatsoever rather a person of ordinary skill in the art would understand claim 1 to encompass the use of a mutated polymerase where the mutation is relative to wild type. The '985 patent does not teach the use of such a mutated polymerase nor does the Examiner contend that the '985 patent teaches such a polymerase. Accordingly, the '985 patent does not teach each and every element of the claimed invention; therefore, claims 1, 5, 9-11, 17, 19-21, 77 and 78 are not anticipated by this reference.

Rejection under 35 U.S.C. § 103(a)

The Examiner bears the burden of establishing a prima facie case of obviousness (Section 103). Section 2143 of the MPEP states "To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure. In re Vaeck, 947 F. 2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Each of the specific rejections is discussed below in light of this standard.

The Examiner has rejected claims 6-8 under 35 U.S.C. § 103(a) as being unpatentable over the '985 patent in view of Brieba et al. (Biochemistry (2000) 39:919-923). Applicant maintains that the combination of the '985 patent and Breiba et al. does not render the present invention obvious.

The '985 patent describes a SELEX process for identification of nucleic acid ligands to a target where the nucleic acid ligand comprises a modified nucleotide. The '985 patent does not teach the use of a mutated polymerase in the SELEX process. Nor does Brieba remedy this deficiency.

The Examiner asserts that Pieken would be motivated by the Brieba teaching to utilize polymerases with superior properties for incorporation of the desired 2'modified nucleotides. The Examiner states that the Brieba reference teaches that T7 polymerase mutants at position 784 preferentially utilize 2'-OH groups. This teaching would not motivate one skilled in the art to use these Breiba H784 mutant polymerases in the methods of the present invention as 2'-OH is the group that naturally occurs in ribonucleotide triphosphates and is not a modified nucleotide triphosphate. In fact, the abstract of the cited Brieba reference teaches away from the present invention stating with regards to histidine 784 point mutants of T7 RNA polymerase, "We find that while these mutations reduce the activity of the polymerases, they do not significantly reduce the level of ribose discrimination."

Furthermore, Table 2 (page 920) of the Breiba reference shows that none of the tested mutant polymerases namely the H784A, Y639F or the double mutant H784A/Y639F were superior to wild type T7 RNA polymerase in the rate of nucleotide incorporation during transcript elongation. Additionally, the cited Brieba reference is silent on the ability of the disclosed mutant polymerases to incorporate 2'-Ome nucleotide triphosphates. Further, the cited Brieba reference teaches away from the use of 2'-Ome nucleotide triphosphates as the abstract of the Brieba reference indicates that the mutant with alanine at position 784 preferentially utilizes substituents capable of acting as hydrogen bond donors or acceptors. 2'-Ome substituents do not act as hydrogen bond donors or acceptors so would not be thought from the cited reference to be preferred substituents of the H784A mutant. The Brieba further teaches away from the present invention by indicating on page 921 that rank order preference for 2' substituents of the Y639F mutant as well as the double mutant H784A/Y639F is as follows: 2'-OH > 2'-F> 2'-H >2'-NH_2. This rank order preference would not motivate one skilled in the art to use either of the indicated mutant polymerases with 2'-OMe substituents that are much bulkier than 2'- NH_2. Accordingly, without some suggestion of all the claimed elements in this cited art, the disclosure of the Pieken '985 patent does not provide a description from which the present invention obviously flows.

The Examiner has rejected claims 12-16 under 35 U.S.C. § 103(a) as being unpatentable over the '985 patent in view of Sousa et al., U.S. Patent No. 6,107,037 (the '037 patent) Applicant maintains that the combination of the '985 patent and the '037 patent does not render the present invention obvious. As discussed above, the Pieken '985 patent does not teach the use of a mutated polymerase in a SELEX process and therefore does not teach the limitations of claims 1, 5, 9-11, 17, 19-22, 77 and 78 as asserted by the Examiner. The 'Sousa '037 patent does not teach the SELEX method. Furthermore, contrary to the Examiner's assertion Sousa, at column 15, lines 44-48, does not teach the use of manganese and magnesium for transcription, as required by pending claims 12-16, rather Sousa states "Transcription reactions were carried out in 40 mM Tris-Cl pH 8.0, 15 MM $MgCl_2$ and 5mM DTT **or** 20mM Manganese Citrate pH 8.0, 5mM DTT." (emphasis added) While the Examiner further states that due to the teachings of column 22, lines 34-37, the ordinary practitioner would have been motivated to use manganese buffer in optimized concentrations in order to permit incorporation of the modified nucleotides, Applicant respectfully disagrees. As previously stated, claims 12 to 16 relate to the use of manganese and magnesium in the transcription mixture which is not taught in the Sousa '037 patent. Furthermore, lines 37 to 43 of the Sousa '037 patent go on to state that there was a sharp reduction of overall wild type and Y639F polymerase activity with Mn^{++} and that an optimal Mn^{++} that would result in high activity was not identified rather similar activity was found for all concentrations tested. Such a teaching would not motivate an ordinary practitioner to use manganese in transcription reactions of the present invention nor does it suggest that optimization was possible, as it could not be achieved, let alone routine. Accordingly, without some suggestion of all the claimed elements in this cited art, the disclosure of Pieken, does not provide a description from which the present invention obviously flows.

The Examiner has rejected claim 18 under 35 U.S.C. § 103(a) as being unpatentable over the '985 patent in view of Milligan et al. (Methods Enxymol. (1989) 180:51-62). Applicant maintains that the combination of the '985 patent and Milligan et al. does not render the present invention obvious. As discussed above, the Pieken '985 patent does not teach the use of a mutated polymerase in a SELEX process. The Milligan et al. reference also does not teach the use of a mutated polymerase in a SELEX process. The Milligan et al. reference does not teach the use of a mutated polymerase at all. Accordingly, the references cited by the Examiner, alone or

combined, do not teach or suggest all the claim limitations as neither reference teaches the use of a mutated polymerase in the claimed method. Without some suggestion of all the claimed elements in this cited art, the disclosure of Pieken, does not provide a description from which the present invention obviously flows.

The Examiner has rejected claims 79-96 under 35 U.S.C. § 103(a) as being unpatentable over the Pieken '985 patent in view of the Sousa '037 patent and further in view of Milligan et al. (Methods Enxymol. (1989) 180:51-62). Applicant maintains that the combination of the '985 patent, the '037 patent and Milligan et al. does not render the present invention obvious.

The Examiner is silent as to the basis of this rejection for claims 79. Accordingly, the Examiner has not met his burden of establishing a prima facie case of obviousness for claims 79 and Applicant respectfully requests clarification as to the basis of the rejection of this claim. All of claims 80 through 87 depend from claims that require the combination of both magnesium and manganese during transcription with a polymerase comprising a Y639F mutation. The Pieken '985 patent does not teach the use of a mutated polymerase nor the use of a combination of both magnesium and manganese during transcription. As discussed above, the Sousa '037 patent does not teach the SELEX method nor the use of the combination of both manganese and magnesium during transcription. All of claims 88 through 96 require the use of both manganese and magnesium during transcription with a polymerase comprising Y639F and H784A mutations. Neither the Pieken '985 patent nor the Sousa '037 patent teach the use of a polymerase comprising both a Y639F and a H784A mutation. Furthermore, as discussed above neither the Pieken '985 patent nor the Sousa '037 patent teach or suggest the use of both manganese and magnesium during transcription.

The Milligan reference does not rectify the deficiencies in the Pieken '985 patent and Sousa '037 patent for claims 80 or 89 as the Milligan reference does not teach or suggest the use of mutated polymerase in the SELEX method, let alone the use of magnesium and manganese during transcription with a T7 mutant polymerase comprising a Y639F or both a Y639F and a H784A mutation. Without some suggestion of all the claimed elements in this cited art, the disclosure of Pieken, does not provide a description from which the present invention obviously flows.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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